

Application No. 10/076,071  
Amendment dated October 3, 2007  
Reply to Office Action dated April 4, 2007

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

Claims 1-530 (Canceled).

531. (Currently amended) A method of treating an angiogenic disease or condition in an animal comprising administering to the animal an amount of a metal-binding peptide which does not have a metal ion bound to it or of a physiologically-acceptable salt of the peptide, the amount of the peptide or salt which is administered to the animal being effective to inhibit angiogenesis, the sequence of the peptide being:

$$P_1 - P_2,$$

wherein:

$P_1$  is:

$Xaa_1$   $Xaa_2$  His or

$Xaa_1$   $Xaa_2$  His  $Xaa_3$ ,

the  $P_1$  portion of the peptide being linear;

$P_2$  is  $(Xaa_4)_n$ ;

$Xaa_1$  is the N-terminal amino acid of the peptide, the only substituents on the  $\alpha$ -amino group of  $Xaa_1$  are hydrogen, and  $Xaa_1$  is glycine, alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or  $\alpha$ -hydroxymethylserine;

$Xaa_2$  is alanine,  $\beta$ -alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or  $\alpha$ -hydroxymethylserine;

$Xaa_3$  is glycine, alanine, valine, lysine, arginine, ornithine, aspartic acid, glutamic acid, asparagine, glutamine or tryptophan; and

$P_2$  is an amino acid sequence which comprises the sequence of a metal binding site, and

P<sub>2</sub> contains no more than 10 amino acids

~~Xaa<sub>1</sub> is any amino acid; and~~

~~— n is 0-10.~~

532. (Previously presented) The method of Claim 531 wherein:

Xaa<sub>1</sub> is glycine, alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, glutamic acid, lysine, hydroxylysine, histidine, arginine, or  $\alpha$ -hydroxymethylserine, and

Xaa<sub>2</sub> is alanine, valine, leucine, isoleucine, threonine, serine, asparagine, glutamine, cysteine, methionine, lysine, hydroxylysine, histidine, arginine, or  $\alpha$ -hydroxymethylserine.

533. (Previously presented) The method of Claim 531 wherein Xaa<sub>1</sub> is aspartic acid, glutamic acid, arginine, threonine or  $\alpha$ -hydroxymethylserine.

534. (Previously presented) The method of Claim 531 wherein Xaa<sub>2</sub> is alanine, valine, leucine, isoleucine, threonine, serine, asparagine, methionine, histidine or  $\alpha$ -hydroxymethylserine.

535. (Previously presented) The method of Claim 531 wherein Xaa<sub>3</sub> is lysine.

536. (Previously presented) The method of Claim 531 wherein:

Xaa<sub>1</sub> is aspartic acid, glutamic acid, arginine, lysine, threonine, serine or  $\alpha$ -hydroxymethylserine,

Xaa<sub>2</sub> is alanine, valine, leucine, isoleucine, threonine, serine, asparagine, methionine, histidine or  $\alpha$ -hydroxymethylserine, and

Xaa<sub>3</sub>, when present, is lysine.

537. (Previously presented) The method of Claim 536 wherein Xaa<sub>1</sub> is aspartic acid or glutamic acid and Xaa<sub>2</sub> is alanine, valine, leucine, isoleucine, threonine, serine or  $\alpha$ -hydroxymethylserine.

538. (Previously presented) The method of Claim 537 wherein Xaa<sub>2</sub> is alanine, valine, leucine or isoleucine.

539. (Previously presented) The method of Claim 538 wherein P<sub>1</sub> is Asp Ala His or Asp Ala His Lys.

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540. (Previously presented) The method of Claim 539 wherein P<sub>1</sub> is Asp Ala His Lys.

541. (Previously presented) The method of Claim 536 wherein Xaa<sub>1</sub> is arginine, lysine, threonine, serine or  $\alpha$ -hydroxymethylserine, and Xaa<sub>2</sub> is alanine, valine, leucine, isoleucine, threonine, serine or  $\alpha$ -hydroxymethylserine.

542. (Previously presented) The method of Claim 541 wherein P<sub>1</sub> is Thr Leu His, HMS HMS His or Arg Thr His.

543-546. (Cancelled)

547. (Currently amended) The method of Claim 531 ~~Claim 546~~ wherein P<sub>2</sub> comprises one of the following sequences:

(Xaa<sub>4</sub>)<sub>m</sub> Xaa<sub>5</sub> Xaa<sub>2</sub> His Xaa<sub>3</sub>, or

(Xaa<sub>4</sub>)<sub>m</sub> Xaa<sub>5</sub> Xaa<sub>2</sub> His,

wherein:

Xaa<sub>4</sub> is any amino acid;

m is 0-5; and

Xaa<sub>5</sub> is an amino acid having a free side-chain -NH<sub>2</sub>, and (Xaa<sub>4</sub>)<sub>m</sub>, if present, or P<sub>1</sub> is attached to Xaa<sub>5</sub> by means of the side-chain amino group.

548. (Previously presented) The method of Claim 547 wherein Xaa<sub>5</sub> is Orn or Lys.

549. (Canceled)

550. (Currently amended) The method of Claim 531 ~~Claim 546~~ wherein P<sub>2</sub> comprises a sequence which binds Cu(I).

551. (Previously presented) The method of Claim 550 wherein P<sub>2</sub> comprises one of the following sequences:

Met Xaa<sub>4</sub> Met,

Met Xaa<sub>4</sub> Xaa<sub>4</sub> Met,

Cys Cys,

Cys Xaa<sub>4</sub> Cys,

Cys Xaa<sub>4</sub> Xaa<sub>4</sub> Cys,

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Met Xaa<sub>4</sub> Cys Xaa<sub>4</sub> Xaa<sub>4</sub> Cys,  
Gly Met Xaa<sub>4</sub> Cys Xaa<sub>4</sub> Xaa<sub>4</sub> Cys [SEQ ID NO:7],  
Gly Met Thr Cys Xaa<sub>4</sub> Xaa<sub>4</sub> Cys [SEQ ID NO:8],  
Gly Met Thr Cys Ala Asn Cys [SEQ ID NO:9], or  
 $\gamma$ -Glu Cys Gly.

552. (Previously presented) The method of Claim 551 wherein P<sub>2</sub> is Gly Met Thr Cys Ala Asn Cys [SEQ ID NO:9].

553-554. (Canceled)

555. (Currently amended) The method of Claim 531 wherein at least one of the amino acids of P<sub>1</sub> other than  $\beta$ -alanine or glycine, when present, is a D-amino acid.

556-557 (Canceled)

558. (Currently amended) The method of Claim 531 or 555 wherein at least one of the amino acids of P<sub>2</sub> other than  $\beta$ -alanine or glycine, when present, is a D-amino acid.

559. (Canceled)

560. (Currently amended) The method of Claim 531 ~~559~~ wherein the terminal -COOH of P<sub>1</sub>-P<sub>2</sub> is substituted to produce -COR<sub>2</sub>, wherein R<sub>2</sub> is -NH<sub>2</sub>, -NHR<sub>1</sub>, -N(R<sub>1</sub>)<sub>2</sub>, -OR<sub>1</sub>, or -R<sub>1</sub>, wherein R<sub>1</sub> is an alkyl, aryl or heteroaryl.

561-568. (Canceled)

569. (Currently amended) The method of ~~any one of Claims 531-542, 544-548, 550-555, 558-568 or 577-580~~ Claim 531 wherein the angiogenic disease or condition is a neoplastic disease, a connective tissue disorder, psoriasis, an ocular angiogenic disease, a cardiovascular disease, a cerebral vascular disease, hemophiliac joints, an immune disorder, a benign tumor, hypertrophy, endometriosis, polyposis, or obesity.

570. (Previously presented) The method of Claim 569 wherein the angiogenic disease or condition is a neoplastic disease.

571. (Previously presented) The method of Claim 570 wherein the neoplastic disease is a tumor.

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572. (Previously presented) The method of Claim 571 wherein the tumor is located in the bladder, brain, breast, kidney, liver, pancreas, lung, cervix, ovary, prostate, stomach, intestines, colon, rectum, or uterus.

573. (Previously presented) The method of Claim 570 wherein the neoplastic disease is tumor metastasis.

574. (Previously presented) The method of Claim 569 wherein the angiogenic disease or condition is psoriasis.

575. (Previously presented) The method of Claim 569 wherein the angiogenic disease or condition is an ocular angiogenic disease.

576. (Previously presented) The method of Claim 575 wherein the ocular angiogenic disease is macular degeneration.

577-580. (Canceled)

581. (New) The method of any one of Claims 550-552 wherein P<sub>1</sub> is Asp Ala His or Asp Ala His Lys.